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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/598,274	06/21/2000	Christopher John Wraight	AP32556-071838	6407

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EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/598,274	WRAIGHT ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,46,49-60,64-77,79,80 and 82-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46,49-60,64-77,79,80 and 82-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Double Patenting

The rejection of record of claims 45-60 and 64-75 set forth in the prior Office Action (mailed 05-29-01) under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,929,040 is withdrawn, in response to the terminal Disclaimer filed 08-05-02.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 76, 77, 79, 80 and 82-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of US Patent No. 6,284,741, which issued from Application No. 09/199,926 on September 4, 2001. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to nucleic acids and compositions comprising antisense directed to IGFBP-2 or -3 which would be encompassed in the nucleic acids and pharmaceutical compositions of antisense claimed in US Patent No. 6,284,741.

Applicant has not provided any arguments to traverse the rejection of record set forth as a provisional rejection over claims 30-36 of co-pending Application No. 09/199,926 (now issued as claims 1-6 of US Patent No. 6,284,741), set forth in the prior office action (mailed 05-29-01).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45, 46, 49-60, 64-77, 79, 80 and 82-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45, 51-60, 64, 66-76, 79, 80 and 82-87 are indefinite due to the recitation "chemical analogue". One skilled in the art would not know what compounds are encompassed by the term "chemical analogue" because the metes and bounds of this

term are unclear. For example, what changes and to what degree can a compound differ from the claimed oligonucleotide and still be considered a "chemical analogue", does the compound need to have the same activity, does the compound need to be a nucleic acid, does the sequence need to remain the same or can a number of sequence changes be made, etc. Claims 46, 49, 50, 65, 77 are indefinite for the same reasons due to dependence on claims 45, 64, or 76.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 76 and 79 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Baserga et al.(U.S. Patent No. 5,643,788).

Baserga et al. disclose an 18 mer nucleic acid analogue of the instantly claimed SEQ ID NO:12 (SEQ ID NO:4 of Baserga et al.) capable of inhibiting IGF-I mediated cell proliferation, and further disclose this nucleic acid in a pharmaceutically acceptable carrier. Therefore, Baserga et al. anticipates claims 76 and 79.

Claims 76 and 79 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Delafontaine.

Delafontaine discloses a 20-mer DNA analogue of SEQ ID NO:12 (SEQ ID NO:1 of Delafontaine). Delafontaine further discloses this oligonucleotide in a pharmaceutically acceptable carrier. The nucleic acid disclosed by Delafontaine would be expected to inherently be capable of inhibiting IGF-I mediated cell proliferation. Therefore, Delafontaine anticipates claims 76 and 79.

Claims 76 and 79 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Low et al. (WO 98/22579).

Low et al. (WO 98/22579) disclose an 18 mer DNA analogue of the instantly claimed SEQ ID NO: 12 (SEQ ID NO:1 of Low et al.). Low et al. further disclose their oligonucleotide in a pharmaceutically acceptable carrier. The nucleic acid disclosed by Low et al. would inherently be capable of inhibiting IGF-I mediated cell proliferation. Therefore, Low et al. anticipates claims 76 and 79.

Claims 76 and 79 are maintained as rejected under 35 U.S.C. 102(e) as being anticipated by Low et al. (U.S. Patent No. 6,071,891). Low et al. disclose an 18 mer DNA analogue of the instantly claimed SEQ ID NO: 12 (SEQ ID NO:1 of Low et al.). Low et al. further disclose their oligonucleotide in a pharmaceutically acceptable carrier. The nucleic acid disclosed by Low et al. would inherently be capable of inhibiting IGF-I mediated cell proliferation. Therefore, Low et al. anticipates claims 76 and 79.

Claims 45, 46, 49, 50, 51, 54, 64-66 and 69 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Werther et al. (reference WO 96/01636 on PTO form 1449, filed March 16, 2001).

Werther et al. disclose methods of treatment for proliferative and inflammatory skin disorders, including psoriasis, using an antisense oligonucleotide consisting of SEQ ID NO: 10 (SEQ ID NO:10 of Werther et al.), which is an 18 mer DNA analogue of SEQ ID NO:14, in a pharmaceutically acceptable carrier. Therefore, Werther et al. anticipates claims 45-51, 54, 61-66, 69, 76, 78 and 81.

Response to Arguments

Applicant's arguments filed October 18, 2001 have been fully considered but they are not persuasive.

In response to the rejection of record of 61-63, 76 and 79 under 35 USC 102 (b) or (e), set forth in the Office action mailed 05-29-01, as anticipated by Baserga et al., Delafontaine et al., Low et al. (WO 98/22579) or Low et al. (US 6,071,891) Applicant argues that the term "chemical analogues" is defined in the specification to include nucleic acids in which a base, nucleotide, nucleoside, or phosphate backbone is modified, but the number of bases is not changed. Applicant points to page 25, lines 13-24 for the definition of "chemical analogue". Applicant states that it is clear from this definition that "chemical analogue" does not extend to a change in the number or sequence of bases. Applicant applies these same arguments to traverse the rejection of record of claims 45-51, 54, 61-66, 69, 76, 78 and 81 under 35 USC 102(b) as anticipated by Werther et al. (WO 96/01636) for methods of treatment using an 18-mer

DNA analogue of SEQ ID NO:14. Applicant has not provided any arguments to traverse the rejection of record of claims 45-51, 54, 61-66, 69, 76, 78 and 81 under 102(b) as anticipated by Werther et al. (WO 96/01636) as it applies to methods of treatment of a skin disorder using an antisense molecule consisting of SEQ ID NO:10.

These arguments have been considered to the extent that they read on the rejections of record of claims 45, 46, 49, 50, 51, 54, 64-66, 69, 76 and 79 under 102 (b) or (e), set forth herein, but they have not been found to be persuasive. The definition for "chemical analogue" provided in the specification at page 25 is not a limiting definition as it states that "chemical analogue of a nucleic acid molecule includes reference to a modified base, nucleotide, nucleoside or phosphate backbone" (emphasis added). This definition does not limit the term "chemical analogue" to these particular modifications. There is no statement to exclude a change in the bases or number of bases from the term "chemical analogue". The specification contemplates embodiments which require addition of bases to the specific sequences claimed, for example, the specification discusses embodiments wherein the antisense molecules are extended to become catalytic RNAs, for example, as a ribozyme or minizyme (see for example, page 27, last paragraph). Given the unclear metes and bounds of the term "chemical analogue", and the non-limiting definition of this term in the specification, "chemical analogue" would encompass analogues of the claimed sequences which are chemically modified to include additional bases.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45, 46, 50, 52, 64, 65 and 67 are maintained as rejected under 35 U.S.C. 103(a) as being unpatentable over Werther et al. (U.S. Patent No. 5,929,040, cited on PTO form 1449, filed September 25, 2000) in view of Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, or Baserga et al.

Werther et al. teach methods of treatment for psoriasis and proliferative skin disorders in a mammal, including a human, as claimed, using antisense which inhibits IGF-I. Werther et al. do not teach their methods of treatment using the specific antisense sequences claimed, or chemical analogues of said sequences.

Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, or Baserga et al. each teach antisense which inhibits IGF-I, which are chemical analogues of the instantly claimed SEQ ID NO:12.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to ameliorate the effects of psoriasis, or other proliferative or inflammatory skin disorder, in a mammal using the methods taught by Werther et al. using the antisense oligonucleotides taught by Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, or Baserga et al. because Werther et al. teach that their methods can be practiced with generally any antisense molecule which inhibits IGF-I. One of ordinary skill in the art would have been motivated to practice the methods taught by Werther et al. using the antisense oligonucleotides taught by Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, or Baserga et al. because Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, or Baserga et al. each teach that their oligonucleotides are effective inhibitors of IGF-I in cells and are useful as pharmaceuticals directed to treat IGF-I mediated diseases.

Therefore, at the time the instant invention was made, the invention of claims 45, 46, 50, 52, 64, 65 and 67 would have been obvious as a whole to one of ordinary skill in the art, absent evidence to the contrary.

Response to Arguments

Applicant's arguments filed October 18, 2001 have been fully considered but they are not persuasive. In response to the rejection of record of claims 45-50, 52, 64, 65 and 67 under 35 USC 103(a) set forth in the prior Office action (mailed 05-29-01) Applicant argues that the references do not teach all of the limitations in the claims, specifically,

that none of the references applied teach an antisense molecule of SEQ ID NO:12 or a chemical analogue thereof. These arguments have been considered to the extent that they read on the rejection of claims 45, 46, 50, 52, 64, 65 and 67, set forth herein, but they have not been found to be persuasive. As set forth in the rejection of record, Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, and Baserga et al. each teach antisense which inhibits IGF-I, which are chemical analogues of the instantly claimed SEQ ID NO:12. The definiton of the term "chemical analogue thereof" does not limit the term "chemical analogue" and, therefore, the antisense taught by Low et al. (U.S. Patent No. 6,071,891), Low et al. (WO 98/22579), Delafontaine, and Baserga et al. are encompassed in the term "chemical analogue" of SEQ ID NO:12.

Conclusion

Any rejection of record not repeated herein is considered to be withdrawn.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
October 28, 2002

SEAN McGARRY
PRIMARY EXAMINER
1635